AGE-RELATED MACULAR DEGENERATION (AMD)

AMD is the leading cause of vision loss in developed countries, and accounts for 8.7% of visual impairment worldwide. AMD is caused by a combination of genetic and environmental factors with age being the greatest risk factor. In the United States, AMD affects 7 percent of people age 60-69 and 35 percent of people age 80 and older (National Institutes of Health). AMD occurs in two forms: dry (nonneovascular) and wet (neovascular or exudative). Ninety percent of all people with AMD have the dry type, which includes the early and intermediate stages of AMD, as well as the advanced form known as geographic atrophy. The wet form affects 10 percent of all people with AMD, and accounts for 50 percent of legal blindness from the disease.

**Estimating Risk of AMD Progression**

The Age-Related Eye Disease Study (AREDS) 9-step severity scale and the simplified 5-step severity scale use drawn-size and pigmenitary abnormalities to determine a risk score upon clinical examination.

- Small: <63 μm
- Intermediate (black arrow): 63-124 μm
- Large (green arrow): 125*-249 μm
- Very large (blue arrow): >250 μm

Adapted from Age-Related Eye Disease Study report no. 17

**AREDS Risk Factor Scoring System**

- +2 For the eye that has neovascular AMD
- +1 If neither eye has large drusen, but both eyes have intermediate drusen
- +1 For each eye with pigment abnormalities
- +1 For each eye with large drusen

The Age-Related Eye Disease Study (AREDS) 9-step Progression Estimating Risk of AMD

- Number of drusen
- Visual acuity test
- Dilated eye exam
- Self-examination (e.g., Amsler grid)

AREDS Simplified Severity Scale

<table>
<thead>
<tr>
<th>5-year rates of progression to advanced AMD</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5%</td>
<td>3%</td>
<td>12%</td>
<td>25%</td>
<td>50%</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Age-Related Eye Disease Study report no. 18

**AMD Treatment Guidelines**

Risk Factors for Progression

- Cigarette smoking
- Family history
- History of cardiovascular disease
- Caucasians, especially women
- Dry AMD in one or both eyes

Dietary Recommendations

- Multivitamins (with antioxidants)
- Smoking cessation
- Regular exercise

**MANAGEMENT OF AMD**

**Early AMD (Dry AMD)**

- Screen for the signs and symptoms of AMD
- Wear UV protective sunglasses
- Get a dilated eye exam

**Intermediate AMD (Dry AMD)**

- Regular monitoring for progression
- Multivitamins with antioxidants
- Smoking cessation
- Regular exercise
- Healthy diet

**Neovascular AMD (Wet AMD)**

- Regular monitoring for disease activity
- Treat with anti-VEGF treatments
- Wear UV protective sunglasses

For a list of indications, including neovascular glaucoma and retinopathy of prematurity.

**VGF Drugs**

- Intraocular VEGF inhibitors
- Systemic VEGF inhibitors

**Anti-VEGF**

- Anti-VEGF treatments have been shown to halt vision loss in more than 90 percent of patients with AMD and to improve vision in one-third.

**VGFInhibitor**

- VEGF inhibitors hold potential for a greater list of indications, including neovascular glaucoma and retinopathy of prematurity.

**VGF Pharmacology**

- VEGF inhibitors have been used to treat, and save vision for patients with AMD and macular edema following retinal vein occlusion. Prior to these developments, neovascular AMD caused 90 percent of AMD-related blindness. With today’s treatments, vision loss can now be avoided in many patients. In fact, up to one-third of neovascular AMD patients treated with anti-VEGF drugs now experience significant improvements in visual acuity. These advancements dramatically improved the outlook for many patients. However, our work continues as we strive to better understand the pathogenesis of AMD and to develop more patient-friendly treatments that aim to prevent retinal disease and preserve vision. We are now poised in 2011, our department underwent a significant milestone when Mass. Eye and Ear joined forces with Schepens Eye Research Institute. This exciting union integrated the efforts of our 100+ faculty and significantly enhanced our bench-to-bedside bandwidth by blending our unique strengths in bench and translational research. Today, collaborations abound across the department, leveraging advances in biotechnology and human genetics that keep our efforts at the forefront of cutting-edge retinal research.

We hope you enjoy this issue of Eye Insights, which explores how far we’ve come over the last decade in bringing sight-saving anti-VEGF treatments to patients with AMD, diabetic macular edema, and retinal vein occlusion, and highlights new efforts that are underway. As always, we hope you find Eye Insights to be a useful tool in your patient’s armamentarium.

Sincerely,

Joan W. Miller, MD, FARVO
Henry Willard Williams Professor of Ophthalmology
Chief, Harvard Medical School Department of Ophthalmology
Chair, Harvard Medical School Department of Ophthalmology colleagues andMass. Eye and Ear joined forces with Schepens Eye Research Institute.

**Inside: High Impact Translational Science**

How biomedical breakthroughs in anti-VEGF research have changed the treatment paradigm, and save vision for patients with retinal disease.

- Annually, 500,000 ophthalmic patients in the United States and over 1 million worldwide are treated with all anti-VEGF agents combined.
- Anti-VEGF treatments have been shown to halt vision loss in more than 90 percent of patients with AMD and to improve vision in one-third.
- VGFInhibitor hold potential for a greater list of indications, including neovascular glaucoma and retinopathy of prematurity.
- VGFInhibitors have been used experimentally to treat over 50 ocular diseases.

See recommended AMD treatment guidelines inside.
So far, two studies provide different recommendations regarding whether genetic testing should be used to guide Age-Related Eye Disease Study (AREDS) or AREDS2 supplemental recommendations. "This is one of the hottest debates at present," Sheehy said. "This includes discussions on the "right,"” noted Joan W. Miller, MD, FCOphth. Chair of the WMs Department of Ophthalmology and Chief of Ophthalmology at Mass. Eye and Ear in General Hospital. "AREDS2 recommendations are reasonable to follow at present," Sheehy said. "However, since we're not quite possible that genetic testing will be used to select the ‘best’ treatment for an individual.”

Multiple Treatment Options

Given the multiple treatment options for neovascular AMD, the selection of medication and treatment modality depends on the type of lesion, as well as the patient’s systemic health, could influence medical, economic considerations. Hazing multiple options has been particularly helpful in treating difficult cases. For example, switching from one anti-VEGF medication to another has been shown to be effective in recurrent and refractory choroidal neovascularization. Photodynamic therapy (PDT) with verteporfin is still an effective method of treating recurrent cases. Moreover, a multitarget, randomized controlled trial that showed that combination therapy (PDT with an anti-VEGF agent) may be an effective approach for treating polypoidal choroidal vasculopathy (PCV), while a retrospective review demonstrated promising results using triple therapy (PDT with an anti-VEGF agent plus a steroid for PCV).